Lymphoma And Pseudolymphoma

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I. T-cell lymphoma
   - MF: patch stage
     - Patchy to band-like lichenoid infiltrate of lesional lymphocytes
     - Papillary dermal fibrosis
     - Epidermotropism:
       • Lymphocytes within the epidermis
       • Lymphocytes align along dermal-epidermal junction
       • Lymphocytes in epidermis with “halo”
       • Larger lymphocytes in epidermis
       • Collections of lymphocytes (Pautrier’s collections)
   - Immunophenotype
     - Usually CD4+ T-lymphocytes
     - Sometimes CD8+ with same clinical course as CD4+
   - Diagnosis of patch-stage MF often challenging
     • Role for ancillary testing?
     • Loss of pan-T-cell antigens (CD2,5,7)
       • Somewhat controversial
       • Can be found in inflammatory conditions
     • Detection of a T-cell clone
       • Frequency of clones in early MF ~ 70%
       • PLEVA 100%; Contact dermatitis 14%
• Identification of the identical clone at different sites increases sensitivity and specificity

• Best diagnostic maneuver if first biopsy not diagnostic. More biopsies!!

• If patch most likely clinically, multiple shave biopsies

• If plaque or tumor stage possible, combination of shaves of likely patches and punches of deeper lesion

• Bottom line: At least 2-3 biopsies, broad shaves optimal. Consider T-cell clonality testing from two biopsies

  – MF- Tumor
    – Diffuse infiltrate of atypical lymphocytes in reticular dermis
    – Cytologically atypical features often quite marked
    – Epidermotropism often diminishes

  - Sézary syndrome
    • Triad:
      – Neoplastic lymphocytes in skin → erythroderma
      – Neoplastic lymphocytes in blood
      – Neoplastic lymphocytes in lymph node

    • Skin histopathology
      – Dense band-like infiltrate of lymphocytes, some of which exhibit epidermotropism
      – Some lymphocytes can be large
      – Evaluation of blood
      – 40% of cases will not show diagnostic features

    – Disorders

  - CD30-positive lymphoproliferative disorders
    • Group of primary cutaneous T-cell lymphomas with expression of CD30 and favorable prognosis
    • Lymphomatoid papulosis (LyP)
    • Primary cutaneous anaplastic large cell lymphoma (ALCL)
    • Borderline cases
• What is CD30?
  – Cytokine receptor belonging to TNF receptor super-family
  – Initially described in Hodgkin lymphoma
  – Marker on activated T and B cells
  – Can be expressed in:
    • CD30-positive lymphoproliferative disorders
    • Hodgkin lymphoma
    • Mycosis fungoides, tumor and plaque stage
    • Diffuse large B-cell lymphoma (rarely)

• Lymphomatoid Papulosis (LyP)
  – Red–brown papules or nodules
  – Typically develop central necrosis
  – Spontaneously resolve within 3-8 weeks
  – Eventuate in dyspigmentation, scarring or no residuum
  – Lesions in different stages common
  – In ~ 20% of patients, concomitant lymphoma, usually MF or Hodgkin lymphoma
  – 5 types: A, B, C, D, E
  – Lymphomatoid papulosis (LyP) – Type A
    • Wedge-shaped infiltrate
    • Clusters or scattered large atypical cells admixed with small lymphocytes, histiocytes, and granulocytes
    • +/-Epidermotropism
    • CD30+
  – LyP Type C
    • Sheets of atypical large cells
    • A small number of admixed small lymphocytes and granulocytes
    • CD30+
  – Type D LyP
    • Histopathology
• Wedge-shaped infiltrate of atypical lymphocytes in dermis with admixed small lymphocytes and granulocytes
• Marked epidermotropism
• Immunophenotype
  • CD30+/CD3+
  • CD4-/CD8+

- Anaplastic large cell lymphoma (ALCL)
  • Clinical: Solitary/localized nodules or tumors that do not self-resolve. Often ulcerated and 3 cm or more in diameter
  • Histopathology:
    - Diffuse sheets of large and atypical lymphocytes
    - Epidermis ulcerate
    - CD30 positive
    - Follicle center
    - Diffuse large B-cell lymphoma, leg type

II. B-cell lymphomas
- Primary cutaneous marginal zone lymphoma: Histopathology
  • Dermal-based infiltrate, epidermal spared
  • Non-neoplastic secondary lymphoid follicles
  • Neoplastic cells at periphery – small cells
    • Marginal zone cells: centrocyte-like cells resembling cells of the marginal zone
    • Plasma cells and plasmacytoid lymphocytes
  • Dutcher bodies – pseudo-intranuclear inclusions in plasma cells
  • Monoclonal plasma cells
- Primary cutaneous follicle center lymphoma
  • Dermal based infiltrate - epidermis spared
  • Follicular, diffuse or mixed pattern
  • Follicular - nodules within the dermis composed of neoplastic lymphoid follicles
• Small centrocyte and centroblast-like cells
• Reduced or absent mantle zones
• Lack of tingible body macrophages
• Primary cutaneous follicle center lymphoma: Immunophenotype
  • CD21 labels follicular dendritic cell networks of neoplastic lymphoid follicles
  • Positive labeling with Bcl-6 and CD10 in CD21-positive foci and beyond
  • Ki-67 proliferation rate usually less than 75% in the CD21 labeling neoplastic lymphoid follicles
• Primary cutaneous follicle center lymphoma – diffuse pattern
  • Diffuse infiltrates within the dermis of centrocytes and centroblasts
  • Often extends into the subcutaneous fat
  • Immunophenotype
  • Bcl-6, CD10 diffuse staining
  • CD21 follicular dendritic cells networks usually absent

- Diffuse large B-cell lymphoma, leg type
  • Histopathology
    – Dense, diffuse infiltrates in dermis and subcutis
    – Usually epidermis spared
    – Sheets of large cells – both centroblasts and immunoblasts
    – Mitoses frequent
    – Diffuse large B-cell lymphoma, leg type - immunophenotype
      • CD20+/bcl-2+/MUM-1+
      • Sometimes bcl-6 positive

III. B-cell pseudolymphoma
• Cutaneous lymphoid hyperplasia, most common type
• Nodules of reactive lymphoid follicles with germinal centers in the dermis
• Intact mantles
• Tingible body macrophages
• High Ki-67 rate of proliferation
• Bcl-6 and CD10 staining only in intrafollicular areas
• Cutaneous lymphoid hyperplasia
• Clonality can help with ddx
• Majority of cases of FCL: Monoclonal rearrangement of the immunoglobulin heavy chain genes